

In the Specification

On page 7, please amend the second paragraph as follows:

The following characteristics were demonstrated:

- The Sequences of the cDNA clones contain an ORF of 1011 nucleotides coding for a polypeptide of 336 amino acids shown in figure 1b.
- This protein has two P domains.
- Other than the P domains, no significant alignment was seen between TWIK-1 and K⁺ channel recently cloned in yeast and which also has two P domains (Ketchum, K.A., et al., 1995, *Nature*, 376, 690-695).
- Analysis of the hydrophobicity of TWIK-1, shown in figure 1c, reveals the presence of four transmembranal domains, designated ~~T1 to T4~~M1 to M4.
- By placing the NH2 end on the cytoplasmic surface, in accordance with the absence of signal peptide, one obtains the topology model shown in figure 1c.
- In this model, the two P domains are inserted in the membrane from the exterior in accordance with the known orientation of these loops in the K⁺ channels.
- In addition, the general structural unit of TWIK-1 is similar to the unit that one would obtain by making a tandem of two classical subunits rectifying the entry of a potassium channel. Like a classical inward rectifier, TWIK-1 does not exhibit the highly conserved segment S4 which is responsible for the sensitivity to the membrane potential of the inward rectification of the K⁺ channels of the Kv family.
- A unusual large loop of 59 amino acids is present between M1 and P1, such as to extend the length of the linker M1-P1 of the extracellular side of the membrane.
- A potential site of the N-glycosylation is present in this loop.

- Three consensus sites of phosphorylation are present at the N-terminal (Ser 19 for calcium calmodulin kinase II) and C-terminal (Ser 303 for casein kinase II) ends of the cytoplasmic domains, and in the M2-M3 linker (Thr161 for protein kinase II).

- The alignment of the P domains of an important group of K^+ channels is presented in figure 2a. It shows that the regions constituting the pore selective for K^+ are well conserved including the G residues in position 16 and 18 and three other residues indicating practically exclusively conservative change in positions 7, 14 and 17. It is of interest to note that a leucine residue is present in the place of a tyrosine conserved in position 18 in the P2 domain of TWIK-1, or of a phenylalanine in position of 17 of the P domain of the K^+ channel of type eag.